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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/742,785	12/20/2000	William J. Curatolo	PC10755AJTJ	8464

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	09/742,785	CURATOLO ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *13 September 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,2,12-15,18,25-31,41-44,47,54-59,69-72,75,82-87,92,95,102,104-107,112 and 151-163*.
   Claim(s) withdrawn from consideration: *3-11,19-24,32-40,48-53,60-68,76-81,88-91,96-101,108-111,116-121,128-131 and*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because: Miyajima's NZ-105 is not outside the scope of the claims. Applicant's argument that Miyajima's composition is not a physical mixture is not persuasive because Miyajima does not state that a chemical reaction reaction takes place between the NZ-105 and the concentration enhancing polymer; Miyajima physically combines the drug with the polymer. Dissolution of the NZ-105 and the HPMCAS in an organic solvent and removing the solvent by evaporation do not represent chemical reaction between the HPMCAS and the NZ-105 and the mixture is a physical mixture in view of the absence of chemical reaction in the process. While paragraph [0029] of the published application states mixing the drug and the concentration enhancing polymer by simple dry mixing, wet or dry granulation, paragraph [0029] does not specifically state that the drug and the polymer retain "the same individual physical properties," according to applicant's remarks. However, even if the preceding applicant's remarks about the drug having "the same individual physical properties" were the case, Miyajima does not describe that the NZ-105 does not retain its properties of calcium channel blocker or calcium antagonist in the combination. Furthermore, wet granulation or wet milling involves use of solvent and eventual evaporation of the solvent by drying (see page 1654 of the 18th edition of Remington's pharmaceutical Sciences on wet granulation). Verapamil (DUNN) is not outside the scope of the claims. A solubility in aqueous medium that is "at least 2-fold the solubility of the more soluble of the crystalline hydrochloride salt and the crystalline free base drug form" is relative and does not exclude verapamil because applicant's specification teaches that solubility improved form of a drug includes "1) a crystalline highly soluble form of the drug such as a salt; (2) a high-energy crystalline form of the drug; (3) a hydrate or solvate crystalline form of a drug; (4) an amorphous form of a drug (for a drug that may exist as either amorphous or crystalline); (5) a mixture of the drug (amorphous or crystalline) and a solubilizing agent; or (6) a solution of the drug dissolved in an aqueous or organic liquid" (para. [0024]-[0027], and verapamil and its salts meet the criteria for "solubility improved form." Regarding Okada and applicant's arguments to physical mixture, it is noted as explained above in the case of Dunn, Okada does not describe chemical reaction to occur between the drug and the polymer and Okada does not describe that the drug's pharmacological activity is changed or modified in the composition and as such the effect/property of the diclofenac is the same in the neet form as is in the combination with concentration enhancing polymer. The structure of the dosage form in Okada does not mean that the mixture is not physical. The instant claims do not exclude tablets or capsule. Tablets and capsules are formed from formulations comprising mixtures of ingredients and such mixtures are physical. Applicant's argument regarding physical mixture vs the composition of the cited prior art references has been addressed extensively and the response provided above is applicable to the Bymaster reference since the Bymaster formulation does not constitute chemical reaction, the ingredients are physically put together if that is what applicant means by the term physical or if the physical is attempting to exclude reaction between the drug and the polymer, Bymaster does not describe that the drug and the polymer to undergo any chemical reaction when they are put together. Duloxetine meets what applicant means by solubility-improved form as discussed above and as described in applicant's specification at paragraph [0024]. The rejections under 35 USC 103 over Bymaster and Dunn is not based on hindsight as is discussed in the previous office action and as described above. Verapamil and verapamil-HCl are solubility-improved according to applicant's definition of the term (see above). There is no picking and choosing in Bymaster because there is disclosure of the various polymers (see column 10, lines 61-67), and drug that is solubility-improved according to applicant's definition of "solubility-improved" (paragraph [0024] of the instant application. Applicant increases the solubility of sparingly soluble drug by combining the drug with concentration enhancing polymer. Bymaster combines drug with concentration enhancing polymer of the types recited in the claims as described in the previous rejections. Therefore, Bymaster inherently solves the problem applicant attempts to solve. However, the claims are directed to composition claims and not to the process of solving the problem. But, even if the claims are directed to method of increasing the solubility of sparingly soluble drug by combining the drug with concentration enhancing polymer(s), a prior art that combines a sparingly soluble drug meeting applicant's definition and applicant's recited and disclosed drugs would inherently teach the method.

BP

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SUPERVISORY PATENT EXAMINER